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Attn: Section 8(e) Coordinator (CAP Agreement)

October 15, 1992

88920010305
8E HQ-92-12067

INT

Dear Coordinator:

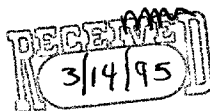
8ECAP-0025

On behalf of the Regulatee and pursuant to Unit II B.1.b. and Unit II C of the 6/28/91 CAP Agreement, E.I. Du Pont de Nemours and Co. hereby submits (*in triplicate*) the attached studies. Submission of this information is voluntary and is occasioned by unilateral changes in EPA's standard as to what EPA now considers as reportable information. Regulatee's submission of information is made solely in response to the new EPA §8(e) reporting standards and is not an admission: (1) of TSCA violation or liability; (2) that Regulatee's activities with the study compounds reasonably support a conclusion of substantial health or environmental risk or (3) that the studies themselves reasonably support a conclusion of substantial health or environmental risk.

The "Reporting Guide" creates new TSCA 8(e) reporting criteria which were not previously announced by EPA in its 1978 Statement of Interpretation and Enforcement Policy, 43 Fed Reg 11110 (March 16, 1978). The "Reporting Guide" states criteria which expands upon and conflicts with the 1978 Statement of Interpretation. Absent amendment of the Statement of Interpretation, the informal issuance of the "Reporting Guide" raises significant due processes issues and clouds the appropriate reporting standard by which regulated persons can assure TSCA Section 8(e) compliance.

For Regulatee,

Mark H. Christman
Counsel
Legal D-7158
1007 Market Street
Wilmington, DE 19898
(302) 774-6443



ATTACHMENT 1

Submission of information is made under the 6/28/91 CAP Agreement, Unit II. This submission is made voluntarily and is occasioned by recent changes in EPA's TSCA §8(e) reporting standard; such changes made, for the first time in 1991 and 1992 without prior notice and in violation of Regulatee's constitutional due process rights. Regulatee's submission of information under this changed standard is not a waiver of its due process rights; an admission of TSCA violation or liability, or an admission that Regulatee's activities with the study compounds reasonably support a conclusion of substantial risk to health or to the environment. Regulatee has historically relied in good faith upon the 1978 Statement of Interpretation and Enforcement Policy criteria for determining whether study information is reportable under TSCA §8(e), 43 Fed Reg 11110 (March 16, 1978). EPA has not, to date, amended this Statement of Interpretation.

After CAP registration, EPA provided the Regulatee the June 1, 1991 "TSCA Section 8(e) Reporting Guide". This "Guide" has been further amended by EPA, EPA letter, April 10, 1992. EPA has not indicated that the "Reporting Guide" or the April 1992 amendment supersedes the 1978 Statement of Interpretation. The "Reporting Guide" and April 1992 amendment substantively lowers the Statement of Interpretation's TSCA §8(e) reporting standard². This is particularly troublesome as the "Reporting Guide" states criteria, applied retroactively, which expands upon and conflicts with the Statement of Interpretation.³ Absent amendment of the Statement of Interpretation, the informal issuance of the "Reporting Guide" and the April 1992 amendment clouds the appropriate standard by which regulated persons must assess information for purposes of TSCA §8(e).

²In sharp contrast to the Agency's 1977 and 1978 actions to soliciting public comment on the proposed and final §8(e) Policy, EPA has unilaterally pronounced §8(e) substantive reporting criteria in the 1991 Section 8(e) Guide without public notice and comment. See 42 Fed Reg 45362 (9/9/77), "Notification of Substantial Risk under Section 8(e): Proposed Guidance".

³A comparison of the 1978 Statement of Interpretation and the 1992 "Reporting Guide" is appended.

Throughout the CAP, EPA has mischaracterized the 1991 guidance as reflecting "longstanding" EPA policy concerning the standards by which toxicity information should be reviewed for purposes of §8(e) compliance. Regulatee recognizes that experience with the 1978 Statement of Interpretation may cause a review of its criteri. Regulatee supports and has no objection to the Agency's amending reporting criteria *provided that* such amendment is not applied to the regulated community in an unfair way. However, with the unilateral announcement of the CAP under the auspices of an OCM enforcement proceeding, EPA has wrought a terrific unfairness since much of the criteria EPA has espoused in the June 1991 Reporting Guide and in the Agency's April 2, 1992 amendment is new criteria which does not exist in the 1978 Statement of Interpretation and Enforcement Policy.

The following examples of new criteria contained in the "Reporting Guide" that is not contained in the Statement of Interpretation follow:

- o even though EPA expressly disclaims each "status report" as being preliminary evaluations that should not be regarded as final EPA policy or intent⁴, the "Reporting Guide" gives the "status reports" great weight as "sound and adequate basis" from which to determine mandatory reporting obligations. ("Guide" at page 20).
- o the "Reporting Guide" contains a matrix that establishes new numerical reporting "cutoff" concentrations for acute lethality information ("Guide" at p. 31). Neither this matrix nor the cutoff values therein are contained in the Statement of Interpretation. The regulated community was not made aware of these cutoff values prior to issuance of the "Reporting Guide" in June, 1991.
- o the "Reporting Guide" states new specific definitional criteria with which the Agency, for the first time, defines as 'distinguishable neurotoxicological effects'; such criteria/guidance not expressed in the 1978 Statement of Interpretation.⁵;
- o the "Reporting Guide" provides new review/ reporting criteria for irritation and sensitization studies; such criteria not previously found in the 1978 Statement of Interpretation/Enforcement Policy.
- o the "Reporting Guide" publicizes certain EPA Q/A criteria issued to the Monsanto Co. in 1989 which are not in the Statement of Interpretation; have never been published in the Federal Register or distributed by the EPA to the Regulatee. Such Q/A establishes new reporting criteria not previously found in the 1978 Statement of Interpretation/Enforcement Policy.

⁴The 'status reports' address the significance, if any, of particular information reported to the Agency, rather than stating EPA's interpretation of §8(e) reporting criteria. In the infrequent instances in which the status reports contain discussion of reportability, the analysis is invariably quite limited, without substantial supporting scientific or legal rationale.

⁵ See, e.g., 10/2/91 letter from Du Pont to EPA regarding the definition of 'serious and prolonged effects' as this term may relate to transient anesthetic effects observed at lethal levels; 10/1/91 letter from the American Petroleum Institute to EPA regarding clarification of the Reporting Guide criteria.

In discharging its responsibilities, an administrative agency must give the regulated community fair and adequate warning to as what constitutes noncompliance for which penalties may be assessed.

Among the myriad applications of the due process clause is the fundamental principle that statutes and regulations which purport to govern conduct must give an adequate warning of what they command or forbid.... Even a regulation which governs purely economic or commercial activities, if its violation can engender penalties, must be so framed as to provide a constitutionally adequate warning to those whose activities are governed.

Diebold, Inc. v. Marshall, 585 F.2d 1327, 1335-36 (D.C. Cir. 1978). See also, Rollins Environmental Services (NJ) Inc. v. U.S. Environmental Protection Agency, 937 F. 2d 649 (D.C. Cir. 1991).

While neither the are rules, This principle has been applied to hold that agency 'clarification', such as the Statement of Interpretation, the "Reporting Guide" nor the April 1992 amendments will not applied retroactively.

...a federal court will not retroactively apply an unforeseeable interpretation of an administrative regulation to the detriment of a regulated party on the theory that the post hoc interpretation asserted by the Agency is generally consistent with the policies underlying the Agency's regulatory program, when the semantic meaning of the regulations, as previously drafted and construed by the appropriate agency, does not support the interpretation which that agency urges upon the court.

Standard Oil Co. v. Federal Energy Administration, 453 F. Supp. 203, 240 (N.D. Ohio 1978), aff'd sub nom. Standard Oil Co. v. Department of Energy, 596 F.2d 1029 (Em. App. 1978):

The 1978 Statement of Interpretation does not provide adequate notice of, and indeed conflicts with, the Agency's current position at §8(e) requires reporting of all 'positive' toxicological findings without regard to an assessment of their relevance to human health. In accordance with the statute, EPA's 1978 Statement of Interpretation requires the regulated community to use scientific judgment to evaluate the significance of toxicological findings and to determining whether they reasonably support a conclusion of a substantial risk. Part V of the Statement of Interpretation urges persons to consider "the fact or probability" of an effect's occurrence. Similarly, the 1978 Statement of Interpretation stresses that an animal study is reportable only when "it contains reliable evidence ascribing the effect to the chemical." 43 Fed Reg. at 11112. Moreover, EPA's Statement of Interpretation defines the substantiality of risk as a function of both the seriousness of the effect and the probability of its occurrence. 43 Fed Reg 11110 (1978). Earlier Agency interpretation also emphasized the "substantial" nature of a §8(e) determination. See 42 Fed Reg 45362, 45363

(1977). [Section 8(e) findings require "extraordinary exposure to a chemical substance...which critically imperil human health or the environment"].

The recently issued "Reporting Guide" and April 1992 Amendment guidance requires reporting beyond and inconsistent with that required by the Statement of Interpretation. Given the statute and the Statement of Interpretation's explicit focus on substantial human or environmental risk, whether a substance poses a "substantial risk" of injury requires the application of scientific judgment to the available data on a case-by-case basis.

If an overall weight-of-evidence analysis indicates that this classification is unwarranted, reporting should be unnecessary under §8(e) because the available data will not "reasonably support the conclusion" that the chemical presents a substantial risk of serious adverse consequences to human health.

Neither the legislative history of §8(e) nor the plain meaning of the statute support EPA's recent lowering of the reporting threshold that TSCA §8(e) was intended to be a sweeping information gathering mechanism. In introducing the new version of the toxic substances legislation, Representative Eckhart included for the record discussion of the specific changes from the version of H. R. 10318 reported by the Consumer Protection and Finance Subcommittee in December 1975. One of these changes was to modify the standard for reporting under §8(e). The standard in the House version was changed from "causes or contributes to an unreasonable risk" to "causes or significantly contributes to a substantial risk". This particular change was one of several made in TSCA §8 to avoid placing an undue burden on the regulated community. The final changes to focus the scope of Section 8(e) were made in the version reported by the Conference Committee.

The word "substantial" means "considerable in importance, value, degree, amount or extent". Therefore, as generally understood, a "substantial risk" is one which will affect a considerable number of people or portion of the environment, will cause serious injury and is based on reasonably sound scientific analysis or data. Support for the interpretation can be found in a similar provision in the Consumer Product Safety Act. Section 15 of the CPSA defines a "substantial product hazard" to be:

"a product defect which because of the pattern of defect, the number of defective products distributed in commerce, the severity of the risk, or otherwise, creates a substantial risk of injury to the public."

Similarly, EPA has interpreted the word 'substantial' as a quantitative measurement. Thus, a 'substantial risk' is a risk that can be quantified, *See*, 56 Fed Reg 32292, 32297 (7/15/91). Finally, since information pertinent to the exposure of humans or the environment to chemical substances or mixtures may be obtained by EPA through Sections 8(a) and 8(d) regardless of the degree of potential risk, §8(e) has specialized function. Consequently, information subject to §8(e) reporting should be of a type which would lead a reasonable man to conclude that some type action was required immediately to prevent injury to health or the environment.

Attachment

Comparison:

Reporting triggers found in the 1978 "Statement of Interpretation/ Enforcement Policy", 43 Fed Reg 11110 (3/16/78) and the June 1991 *Section 8(e) Guide*.

TEST TYPE _____	1978 POLICY <u>CRITERIA EXIST?</u>	New 1991 GUIDE <u>CRITERIA EXIST?</u>
ACUTE LETHALITY		
Oral	N}	Y}
Dermal	N}	Y}
Inhalation (Vapors)	} ⁶	} ⁷
aerosol	N}	Y}
dusts/ particles	N}	Y}
SKIN IRRITATION	N	Y ⁸
SKIN SENSITIZATION (ANIMALS)	N	Y ⁹
EYE IRRITATION	N	Y ¹⁰
SUBCHRONIC (ORAL/DERMAL/INHALATION)	N	Y ¹¹
REPRODUCTION STUDY	N	Y ¹²
DEVELOPMENTAL TOX	Y ¹³	Y ¹⁴

⁶43 Fed Reg at 11114, comment 14:

"This policy statements directs the reporting of specific effects when unknown to the Administrator. Many routine tests are based on a knowledge of toxicity associated with a chemical. Unknown effects occurring during such a range test may have to be reported if they are those of concern to the Agency and if the information meets the criteria set forth in Parts V and VII."

⁷Guide at pp.22, 29-31.

⁸Guide at pp-34-36.

⁹Guide at pp-34-36.

¹⁰Guide at pp-34-36.

¹¹Guide at pp-22; 36-37.

¹²Guide at pp-22

¹³43 Fed Reg at 11112

"Birth Defects" listed.

¹⁴Guide at pp-22

NEUROTOXICITY	N	Y ¹⁵
CARCINOGENICITY	Y ¹⁶	Y ¹⁷
MUTAGENICITY		
<i>In Vitro</i>	Y ¹⁸	Y ¹⁹
<i>In Vivo</i>	Y}	Y}
ENVIRONMENTAL		
Bioaccumulation	Y}	N
Bioconcentration	Y ²⁰	N
Oct/water Part. Coeff.	Y}	N
Acute Fish	N	N
Acute Daphnia	N	N
Subchronic Fish	N	N
Subchronic Daphnia	N	N
Chronic Fish	N	N
AVIAN		
Acute	N	N
Reproductive	N	N
Reproductive	N	N

¹⁵Guide at pp-23; 33-34.

¹⁶43 Fed Reg at 11112
"Cancer" listed

¹⁷Guide at pp-21.

¹⁸43 Fed Reg at 11112; 11115 at Comment 15

"Mutagenicity" listed/ *in vivo* vs *in vitro* discussed; discussion of "Ames test".

¹⁹Guide at pp-23.

²⁰43 Fed Reg at 11112; 11115 at Comment 16.

CAS# 111-36-4

CHEM: Isocyanic acid, butyl ester

TITLE: Acute Inhalation Toxicity

DATE: 12/19/68

SUMMARY OF EFFECTS: LC50 15.6 ppm

Copies to: R. W. Luckenbaugh (6)

E. I. du Pont de Nemours and Company
Haskell Laboratory for Toxicology and Industrial Medicine

HASKELL LABORATORY REPORT NO. 289-68

MR NO. 581-283

Material Tested: Isocyanic Acid, Butyl Ester

Haskell No.: 5732

Material Submitted by: R. W. Luckenbaugh, Industrial and Biochemicals
Department, Agricultural Chemicals Section

Other Codes: IN-17505
N.B. 4652-134

ACUTE INHALATION TOXICITY

Procedure: The compound was metered into a stainless steel T-tube which was heated to 125-150°C to insure vaporization. The vapors were carried into a 16-liter bell jar containing six Chr-CD male rats weighing 252-285 grams by a measured air flow. The chamber atmosphere was analyzed by a gas chromatographic procedure. Exposures lasted four hours.

Rats were held for 30 days after exposure because they were still losing weight 14 days after the exposure.

Results:

Analytical
Concentration
(ppm)

12.5
17.5
22
31.5
53.5

Mortality Rate

During
Exposure

0/6
0/6
0/6
2/6
2/6

14 Day

0/6
2/6
2/6
6/6
6/6

30 Day

2/6
3/6
5/6
6/6
6/6

Clinical Signs

During Exposure: irregular breathing, hyperemia, gasping, pale ears and death; some lacrimation first 10-15 minutes of the exposure

Post-Exposure: 10 to 20 per cent body weight loss during the first day after the exposure; in most cases there were minor weight gains for a few days, then losses again; congestion, rales, red discharge from eyes, priapism, gasping and difficulty in breathing were observed during the 30 days post-exposure

30 Day LC_{50} = 15.6 ppm

Pathology: Histopathologic examinations were performed on tissues from two rats dying during exposure to 53.5 ppm; two rats sacrificed at each of 1 and 2 days post-exposure at the 35 ppm level; one rat 7 days post-exposure at the 35 ppm level; two rats 14 days post-exposure at the 12.5 ppm level and three rats 30 days post-exposure at the 17.5 ppm level.

Grossly, rats dying during exposure had dark red colored, edematous lungs almost twice normal weight. Rats exposed to 35 ppm butylisocyanate for four hours had lung weights near the top of the normal range 1 and 2 days after exposure and approximately $1\frac{1}{2}$ average normal weight 7 days after exposure. Lung weights were still increasing at 14 days and had reached approximately twice average normal weight in 30 days.

The acute necrotizing effect of butylisocyanate on the respiratory system caused necrosis and desquamation of the epithelial lining of the bronchial tree and increased capillary permeability. Edema and in some cases hemorrhage were the result of the vascular damage. In the rats that were killed on recovery days 1 and 2, marked inflammatory cell infiltration was noted in the sub-mucosa of the trachea and bronchial tree. Edema was also prominent in these animals.

Regeneration of the bronchial epithelium in the one 7-day recovery animal was evident and repair was complete in the 14-day recovery animals. In some cases the epithelium had formed folds and papilla-like arrangements that constricted the lumens of the bronchioles. The connective tissue surrounding these air passages was also increased resulting in bronchiolitis fibrosa obliterans and atelectasis.

Also by the 14th day bronchopneumonia become evident. This condition progressed to severe proportions by the 30th recovery day with resulting atelectasis and consolidation of some lobes.

Summary: The LC50, based on 30 days observation period of isocyanic acid, butyl ester, was 15.6 (13.3-18.2) ppm for a four-hour rat exposure. Thus, it should be considered highly toxic by inhalation and inhalation should be avoided. Butyl isocyanate caused a progressive increase in rat lung weight and deaths occurred throughout a 30-day hold period. Some rats were still losing weight 30 days after exposure. A similar lung weight increase after inhalation exposure was observed with 3,4-dichlorophenyl isocyanate (2).

Summary (Cont'd.)

Butyl isocyanate is a highly necrotizing compound when inhaled under the conditions used in this test. Animals that survive the initial exposure are highly susceptible to bronchopneumonia by "opportunistic" bacteria which normally inhabit the respiratory tract of the rat.

- (1) Statistical analysis by method of J. T. Litchfield, Jr., F. Wilcoxon, J. Pharmacol. and Expt'l. Therap., 96, 99 (1949).
- (2) Haskell Laboratory Report No. 38-68; 14-day LC₅₀ for a four-hour exposure = 350 ppm.

Report by:

Figen O. Fayfun
Figen O. Fayfun
Inhalation Toxicology Section

Approved by:

John A. Zapp, Jr.
John A. Zapp, Jr.
Director

FOT/jch

Date: December 19, 1968



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

Mark H. Christman
Counsel
E. I. Du Pont De Nemours and Company
Legal D-7010-1
1007 Market Street
Wilmington, Delaware 19898

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MAY 08 1995

EPA acknowledges the receipt of information submitted by your organization under Section 8(e) of the Toxic Substances Control Act (TSCA). For your reference, copies of the first page(s) of your submission(s) are enclosed and display the TSCA §8(e) Document Control Number (e.g., 8EHQ-00-0000) assigned by EPA to your submission(s). Please cite the assigned 8(e) number when submitting follow-up or supplemental information and refer to the reverse side of this page for "EPA Information Requests" .

All TSCA 8(e) submissions are placed in the public files unless confidentiality is claimed according to the procedures outlined in Part X of EPA's TSCA §8(e) policy statement (43 FR 11110, March 16, 1978). Confidential submissions received pursuant to the TSCA §8(e) Compliance Audit Program (CAP) should already contain information supporting confidentiality claims. This information is required and should be submitted if not done so previously. To substantiate claims, submit responses to the questions in the enclosure "Support Information for Confidentiality Claims". This same enclosure is used to support confidentiality claims for non-CAP submissions.

Please address any further correspondence with the Agency related to this TSCA 8(e) submission to:

Document Processing Center (7407)
Attn: TSCA Section 8(e) Coordinator
Office of Pollution Prevention and Toxics
U.S. Environmental Protection Agency
Washington, D.C. 20460-0001

EPA looks forward to continued cooperation with your organization in its ongoing efforts to evaluate and manage potential risks posed by chemicals to health and the environment.

Sincerely,

Terry R. O'Bryan
Terry R. O'Bryan
Risk Analysis Branch

Enclosure

12067A



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Triage of 8(e) Submissions

Date sent to triage: MAY 09 1995

NON-CAP

CAP

Submission number: 12067A

TSCA Inventory:

Y

N

D

Study type (circle appropriate):

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ECO

AQUATO

Group 2 - Ernie Falke (1 copy total)

ATOX

SBTOX

SEN

w/NEUR

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EPI

RTOX

GTOX

STOX/ONCO

CTOX/ONCO

IMMUNO

CYTO

NEUR

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Notes:

Contractor reviewer:

PR

Date:

4/28/95

CECATS DATA
Submission # BEHQ 1092 -12067 SEQ. ATYPE: INT SUPP FLWPSUBMITTER NAME: E. I. Dupont deNamours and Company

INFORMATION REQUESTED: FLWP DATE:

0501 NO INFO REQUESTED

0502 INFO REQUESTED (TECH)

0503 INFO REQUESTED (VOL ACTIONS)

0504 INFO REQUESTED (REPORTING RATIONALE)

DISPOSITION:

0603 REFER TO CHEMICAL SCREENING

0607 CAP NOTICE

VOLUNTARY ACTIONS:

0601 NO ACTION REQUIRED

0602 STUDIES PLANNED/IN PROGRESS

0603 NOTIFICATION OF WORKING STATUS

0604 LABEL/MSDS CHANGES

0605 PROCESS/HANDLING CHANGES

0606 APP/USE DISCONTINUED

0607 PRODUCTION DISCONTINUED

0608 CONFIDENTIAL

SUB DATE: 10/15/92 OTS DATE: 10/27/92 CSRAD DATE: 03/14/95

CHEMICAL NAME:

CASE#

111-36-4

INFORMATION TYPE:

P F C

INFORMATION TYPE:

P F C

INFORMATION TYPE:

P F C

0201	ONCO (HUMAN)	01 02 04	0216	EPICLIN	01 02 04	0241	IMMUNO (ANIMAL)	01 02 04
0202	ONCO (ANIMAL)	01 02 04	0217	HUMAN EXPOS (PROD CONTAM)	01 02 04	0242	IMMUNO (HUMAN)	01 02 04
0203	CELL TRANS (IN VITRO)	01 02 04	0218	HUMAN EXPOS (ACCIDENTAL)	01 02 04	0243	CHEM/PHYS PROP	01 02 04
0204	MUTA (IN VITRO)	01 02 04	0219	HUMAN EXPOS (MONITORING)	01 02 04	0244	CLASTO (IN VITRO)	01 02 04
0205	MUTA (IN VIVO)	01 02 04	0220	ECO/AQUA TOX	01 02 04	0245	CLASTO (ANIMAL)	01 02 04
0206	REPRO/TERATO (HUMAN)	01 02 04	0221	ENV. OCCURENCE/FATE	01 02 04	0246	CLASTO (HUMAN)	01 02 04
0207	REPRO/TERATO (ANIMAL)	01 02 04	0222	EMERG INCI OF ENV CONTAM	01 02 04	0247	DNA DAM/REPAIR	01 02 04
0208	NEURO (HUMAN)	01 02 04	0223	RESPONSE REQUEST DELAY	01 02 04	0248	PROD/USE/PROC	01 02 04
0209	NEURO (ANIMAL)	01 02 04	0224	PROD/COMP/CHEM ID	01 02 04	0251	MSDS	01 02 04
0210	ACUTE TOX (HUMAN)	01 02 04	0225	REPORTING RATIONALE	01 02 04	0299	OTHER	01 02 04
0211	CHR. TOX (HUMAN)	01 02 04	0226	CONFIDENTIAL	01 02 04			
0212	ACUTE TOX (ANIMAL)	01 02 04	0227	ALLERG (HUMAN)	01 02 04			
0213	SUB ACUTE TOX (ANIMAL)	01 02 04	0228	ALLERG (ANIMAL)	01 02 04			
0214	SUB CHRONIC TOX (ANIMAL)	01 02 04	0239	METAB/PHARMACO (ANIMAL)	01 02 04			
0215	CHRONIC TOX (ANIMAL)	01 02 04	0240	METAB/PHARMACO (HUMAN)	01 02 04			

TRIAGE DATA:

NON-CBI INVENTORY

ONGOING REVIEW

SPECIES

TOXICOLOGICAL CONCERN:

USE:

PRODUCTION:

YES

YES (DROP/REFER)

RAT

LOW

CAS SR

NO

NO (CONTINUE)

MED

(M) (N) (M) (N)

REF: R

HIGH

UNCLASSIFIED

-CPSS- 0927952113

0 0 0 0 0 0 0 0 0 0 0

> <ID NUMBER>

8(E)-12067A

> <TOX CONCERN>

H

> <COMMENT>

ACUTE INHALATION TOXICITY IN MALE RATS IS HIGH CONCERN BASED ON AN LC50 OF 15.6 PPM. DOSE (PPM) AND MORTALITY: 12.5 (2/6), 17.5 (3/6), 22 (5/6), 31.5 (6/6), AND 53.5 (6/6). CLINICAL SIGNS INCLUDED IRREGULAR BREATHING, HYPEREMIA, GASPING, PALE EARS, LACRIMATION, CONGESTION, RALES, RED DISCHARGE FROM EYES, AND PRIAPISM. PATHOLOGIC EXAM REVEALED DARK RED-COLORED, EDEMATOUS LUNGS ALMOST TWICE THE NORMAL WEIGHT, NECROSIS AND DESQUAMATION OF THE EPITHELIAL LINING OF THE BRONCHIAL TREE AND INCREASED CAPILLARY PERMEABILITY, AND MARKED INFLAMMATORY CELL INFILTRATION IN SUB-MUCOSA OF THE TRACHEA AND BRONCHIAL TREE.

\$\$\$\$